



Beyond the Primary Tumor: Malignancy Risk and Evaluation Strategies for ¹⁸F-FDG PET/CT-Detected Incidentalomas

Primer Tümörün Ötesinde: ¹⁸F-FDG PET/BT ile Saptanan İnsidentalomalarda Malignite Riski ve Değerlendirme Stratejileri

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Abstract

Objectives: The increasing use of ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) imaging has led to the frequent detection of incidentalomas. This study aimed to investigate the prevalence, locations, malignancy rates, and clinical evaluations of incidentalomas detected during preoperative staging with ¹⁸F-FDG PET/CT in patients with surgically relevant primary tumors.

Methods: A total of 251 patients who underwent preoperative ¹⁸F-FDG PET/CT imaging between January 2019 and December 2023 were retrospectively analyzed. Incidental uptake sites were classified into six anatomical regions: thyroid, colon, rectum, prostate, cervix/uterus, and breast. Data regarding maximum standardized uptake value (SUV_{max}) values, biopsy status, imaging follow-up, and histopathological outcomes were recorded and compared with population-based incidence data from the literature.

Results: The most frequent incidentalomas were detected in the thyroid (11.6%), followed by cervix/uterus (9.6%), colon (7.6%), prostate (4.4%), breast (2.4%), and rectum (2.0%). Malignancy was confirmed in incidentalomas of the thyroid (85.7%), prostate (83.3%), colon (71.4%), rectum (50.0%), and breast (33.3%). Malignancy rates for the thyroid, breast, colorectal, and prostate groups were significantly higher than population-based estimates ($p<0.05$). No statistically significant correlation was found between SUV_{max} and malignancy status across localization groups.

Conclusion: Incidental findings on ¹⁸F-FDG PET/CT imaging are common and carry a considerable risk of malignancy, particularly in thyroid, prostate, and colorectal sites. Given the observed diagnostic yield, further clinical evaluation, including tissue diagnosis, should be considered in cases with focal uptake, especially when located in high-risk anatomical regions. Awareness of these findings is essential for timely management and appropriate therapeutic decision-making.

Keywords: Incidentaloma, malignancy, preoperative staging, ¹⁸F-FDG PET/CT

Öz

Amaç: ¹⁸F-florodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı tomografi (¹⁸F-FDG PET/BT) kullanımının artması, incidentalomalardan sık tespit edilmesine yol açmıştır. Bu çalışmada, cerrahi açısından anlamlı primer tümörü olan hastalarda preoperatif evreleme sırasında ¹⁸F-FDG PET/BT ile saptanan incidentalomalardan prevalansı, lokalizasyonu, malignite oranları ve klinik değerlendirme süreçleri araştırılmıştır.

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Yöntem: Ocak 2019-Aralık 2023 tarihleri arasında preoperatif ¹⁸F-FDG PET/CT görüntülemesi yapılan toplam 251 hasta retrospektif olarak incelenmiştir. Saptanan incidental tutumlar anatomik olarak altı bölgeye ayrılmıştır: tiroid, kolon, rektum, prostat, serviks/uterus ve meme. İlgili odaklara ait maksimum standart tutum değeri (SUV_{max}) değerleri, biyopsi durumu, görüntüleme takipleri ve histopatolojik sonuçlar kaydedilmiştir ve literatürdeki toplum temelli insidans verileriyle karşılaştırılmıştır.

Bulgular: En sık incidentalomalar tiroidde (%11,6), ardından serviks/uterus (%9,6), kolon (%7,6), prostat (%4,4), meme (%2,4) ve rektumda (%2,0) saptanmıştır. Malignite oranları tiroidde %85,7, prostatta %83,3, kolonda %71,4, rektumda %50,0 ve memede %33,3 olarak belirlenmiştir. Tiroid, meme, kolorektal ve prostat gruplarında saptanan malignite oranları, toplum temelli tahminlere kıyasla anlamlı derecede yüksek saptanmıştır ($p<0,05$). SUV_{max} değerleri ile malignite durumu arasında lokalizasyon grupları genelinde istatistiksel olarak anlamlı bir ilişki saptanmamıştır.

Sonuç: ¹⁸F-FDG PET/CT görüntülemesinde saptanan incidental bulgular yaygın olup özellikle tiroid, prostat ve kolorektal bölgelerde belirgin bir malignite riski taşımaktadır. Tanısal testlerin artışı göz önüne alındığında, odak tutulumu gösteren ve yüksek riskli anatomik bölgelerde yer alan lezyonlarda doku tanısı dahil olmak üzere ileri klinik değerlendirme önerilmelidir. Bu bulgulara yönelik farkındalık, zamanında müdahale ve uygun tedavi kararlarının verilmesi açısından kritik öneme sahiptir.

Anahtar kelimeler: incidentaloma, malignite, preoperatif evreleme, ¹⁸F-FDG PET/CT

Introduction

The term “positron emission tomography (PET)-associated incidental neoplasm (PAIN)” was first described by Katz and Shah (1) in their 2008 publication and refers to a neoplasm incidentally detected during PET/computed tomography (CT) imaging performed for unrelated reasons.

Incidental findings detected on ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) PET/CT are more frequent in patients older than 45 years, with a cumulative incidence ranging from 0.2% to 8.9%. Since FDG uptake is related to cellular glucose transport, it may occur not only in malignancies but also in infections, inflammation, and benign tumors. The prevalence of malignant incidentalomas varies between 1.2% and 1.7% (2).

In patients with a known diagnosis of malignancy, examinations typically focus on the primary disease, which may lead to overlooking a coincident benign or malignant lesion. However, the presence of an additional neoplasm is not negligible, and incidentalomas require further qualified evaluation and clinical investigation.

The aim of this study is to compare the rate of incidentalomas detected among patients hospitalized in the general surgery department with global incidence rates and to evaluate the proportion of patients who underwent further investigation and the distribution of benign and malignant lesions. Based on the data obtained, the study also aims to develop recommendations for clinicians regarding the appropriate management of incidentalomas.

Materials and Methods

Patient Selection

Patients who underwent surgery for a primary malignancy and received ¹⁸F-FDG PET/CT imaging for preoperative staging at the Department of General Surgery, University of Health Sciences Türkiye, Dr. Abdurrahman Yurtaslan

Ankara Oncology Training and Research Hospital, between January 2019 and December 2023 were retrospectively included in this study. Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of University of Health Sciences Türkiye, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital under the (number: 2024-10/148, date: 31.10.2024).

Inclusion criteria for the study were patients aged 18 years or older and patients who underwent ¹⁸F-FDG PET/CT imaging for staging of a primary malignancy within the field of general surgery. Exclusion criteria included patients under 18 years of age; patients whose ¹⁸F-FDG PET/CT findings were attributable to metastasis; patients with inaccessible medical records; patients who were not followed up at our center; and patients who had received treatment targeting the primary tumor before staging.

Data Collection

The following were retrospectively reviewed: demographic characteristics (age and sex) of the patients included in the study; locations of their primary tumors; localizations of the incidentalomas; maximum standardized uptake value (SUV_{max}) of the incidentalomas; whether additional imaging was performed for the incidentalomas and the resulting imaging findings; whether a biopsy was performed for the incidentalomas and, if available, the biopsy results.

Study Design

In the present study, patients with primary tumors falling within the scope of general surgery—specifically those located in the esophagus, stomach, small intestine, colon, liver, gallbladder and biliary tract, pancreas, breast, and thyroid—were included. Based on an initial literature review, patients were grouped by the anatomical localization of incidentalomas, focusing on incidental uptake foci detected in the thyroid, colon, rectum, prostate, and breast. Any focal uptake in these regions that differed from typical patterns was considered suspicious for an incidentaloma.

Following identification of a cervical malignancy during further investigation of incidental uterine uptake in one patient, a uterus–cervix group was added to the classification. For all patients, the following were recorded: whether there was incidental uptake in these regions; the corresponding SUV_{max} values (without applying any threshold); whether further investigations were conducted; the outcomes of these investigations; and whether a biopsy was performed.

The objective of this research was to evaluate the frequency with which incidentalomas are detected on preoperative ^{18}F -FDG PET/CT scans relative to their incidence in the general population, and to quantify the proportion that represent malignant disease. The study sought to raise surgeons' awareness of the clinical significance of incidental findings.

^{18}F -FDG PET/CT

All patients underwent imaging using an integrated PET/CT scanner (Siemens Biograph 6 TruePoint). Prior to the ^{18}F -FDG PET/CT examination, patients fasted for at least 6 hours and serum glucose levels at the time of tracer administration were confirmed to be below 150 mg/dL. ^{18}F -FDG was administered intravenously at a dose of 3.3 MBq/kg (90 $\mu\text{Ci}/\text{kg}$) via an automated infusion system (Intego PET Infusion system). PET and low-dose CT images were acquired in a single session, with the CT performed without intravenous iodinated contrast and covering the region from the skull vertex to the distal thighs. CT images were used for attenuation correction and anatomical localization. All image data were reviewed on a dedicated workstation (Syngovia, Siemens Medical Solutions) in standard planes, including maximum intensity projection views. Both visual assessment and quantitative analysis were performed. For quantitative evaluation, SUV_{max} , normalized to body weight, was manually determined for the primary tumor and relevant regions. All findings were documented in the whole-body ^{18}F -FDG PET/CT report.

Statistical Analysis

The data were analyzed using SPSS version 11.5. Descriptive statistics for categorical variables were expressed as frequency (percentage). For comparisons of numerical variables between two categories of a qualitative variable, the Mann-Whitney U test was used because the assumptions of normality were not met. To evaluate differences in numerical variables across qualitative variables with more than two categories, the Kruskal-Wallis H test was applied. When a significant difference among more than two groups was detected, Bonferroni-adjusted Mann-Whitney U tests were conducted to determine which specific group pairs accounted for the difference.

Associations between categorical variables were analyzed using chi-square test and Fisher's exact test. A one-proportion Z test was used to compare the observed incidence rate in the study population with the known population rate. The risk factors affecting the categorical variable were analyzed using univariate and multivariate logistic regression analyses. A p value of less than 0.05 was considered statistically significant throughout the analyses.

Results

A total of 251 patients who underwent ^{18}F -FDG PET/CT for preoperative staging were included in the present study. The mean age of the patients was 61.68 years, and 72.1% were female. When patients were classified by primary tumor location, 157 (62.5%) had breast cancer, 32 (12.7%) rectal cancer, 21 (8.4%) gastric cancer, 18 (7.2%) colon cancer, 10 (4.9%) esophageal cancer, 9 (3.6%) pancreatic cancer, 2 (0.8%) thyroid cancer, and one patient each (0.4%) had liver or adrenal gland malignancies (Table 1).

Table 2 presents the localization of incidentalomas and tumor-related variables. Significant differences were observed between incidentaloma localization and SUV_{max} , tumor presence, and whether additional imaging was performed ($p=0.001$, $p<0.001$, and $p=0.004$, respectively). The highest mean SUV_{max} was observed in colon incidentalomas, whereas the lowest was observed in breast incidentalomas. Pairwise comparisons revealed that the significant differences in incidentaloma localization across primary tumor types were primarily driven by the following pairs: breast vs. cervix ($p=0.025$), breast vs. rectum ($p=0.004$), breast vs. colon ($p<0.001$), thyroid vs. colon ($p<0.001$), and prostate vs. colon ($p=0.030$).

Table 1. Descriptive data for demographic characteristics

Variables	
Age	Mean \pm SD
	61.68 \pm 13.43
Gender, n (%)	
Female	181 (72.1)
Male	70 (27.9)
Primary tumor localization, n (%)	
Breast	157 (62.5)
Rectum	32 (12.7)
Stomach	21 (8.4)
Colon	18 (7.2)
Esophagus	10 (4.0)
Pancreas	9 (3.6)
Thyroid	2 (0.8)
Liver	1 (0.4)
Adrenal gland	1 (0.4)
SD: Standard deviation	

Incidentaloma rates by anatomical site were: 11.6% in the thyroid, 9.6% in the cervix, 7.6% in the colon, 4.4% in the prostate, 2.4% in the breast, and 2.0% in the rectum. The distribution of incidentaloma locations by primary tumor site is presented in Table 3. All patients with rectal or breast incidentalomas underwent additional imaging, compared with 37.6% of thyroid incidentalomas, 78.9% of colon incidentalomas, 63.6% of prostate incidentalomas, and 70.8% of cervical incidentalomas.

The localization of incidentalomas was compared with prevalence rates reported in the literature. Table 4 presents a comparison of the study findings with population-based rates. Significantly higher detection rates were observed in the thyroid, breast, colorectal, and prostate groups than in the general population ($p<0.001$, $p<0.001$, $p=0.002$, and $p<0.001$, respectively). The population incidence rates were based on studies by Albano et al. (3) (thyroid), Panareo et al. (2) (breast), Treglia et al. (4) (colorectal), and Mannas et

al. (5) (prostate). No reference data were identified in the literature regarding incidental cervical or uterine findings.

Following advanced evaluation of incidentalomas, the malignancy rates were as follows: 85.7% in the thyroid, 71.4% in the colon, 50.0% in the rectum, 83.3% in the prostate, and 33.3% in the breast.

Table 5 presents the analysis of SUV_{max} values in patients diagnosed with malignancy, stratified by incidentaloma localization. Despite this evaluation, the comparison of SUV_{max} between malignant and benign lesions across different sites did not demonstrate any statistically significant differences. ($p>0.05$) (Table 5).

Risk factors potentially affecting malignancy were evaluated (Table 6). Based on the results of univariate and multivariate logistic regression analyses, no variable was identified as a significant risk factor, either individually or in combination.

Table 2. Comparisons of variables based on incidentaloma localizations

Variables	Incidentaloma localization						p value
	Thyroid	Colon	Rectum	Prostate	Cervix/uterus	Breast	
Incidentaloma, n (%)	29 (11.6)	19 (7.6)	5 (2.0)	11 (4.4)	24 (9.6)	6 (2.4)	<0.001^b
SUV_{max} Mean \pm SD	4.65 \pm 1.94	9.74 \pm 4.85	7.82 \pm 2.09	5.77 \pm 4.01	5.92 \pm 2.75	2.80 \pm 0.96	0.001^a
Additional imaging performed, n (%)	11 (37.9)	15 (78.9)	5 (100.0)	7 (63.6)	17 (70.8)	6 (100.0)	0.004^c
Biopsy, n (%)	7 (24.1)	7 (36.8)	2 (40.0)	2 (18.2)	6 (25.0)	3 (50.0)	0.642^c
Biopsy result, Benign Malign	1 (14.3) 6 (85.7)	2 (28.6) 5 (71.4)	1 (50.0) 1 (50.0)	1 (50.0) 1 (50.0)	1 (16.7) 5 (83.3)	2 (66.7) 1 (33.3)	0.365 ^c

SD: Standard deviation, ^a: Kruskal-Wallis H test, ^b: Chi-square test, ^c: Fisher's exact test, SUV_{max} : Maximum standardized uptake value

Table 3. Incidentaloma distribution based on primary tumor localization

Primary tumor localization	Incidentaloma localization, n (%)					
	Thyroid	Colon	Rectum	Prostate	Cervix/uterus	Breast
Breast	19 (65.5)	6 (31.6)	3 (60.0)	1 (9.1)	19 (79.2)	5 (83.3)
Rectum	3 (10.3)	6 (31.6)	-	3 (27.2)	-	1 (16.7)
Stomach	4 (13.7)	3 (15.7)	-	5 (45.5)	2 (8.3)	-
Colon	1 (3.5)	2 (10.5)	1 (20.0)	1 (9.1)	3 (12.5)	-
Esophagus	1 (3.5)	1 (5.3)	1 (20.0)	1 (9.1)	-	-
Pancreas	1 (3.5)	1 (5.3)	-	-	-	-
Thyroid	-	-	-	-	-	-
Liver	-	-	-	-	-	-
Adrenal gland	-	-	-	-	-	-

Table 4. Incidence rates of incidentaloma localizations

Incidentaloma localization	Incidence rate (%)	Population-based rate (%)	p value
Thyroid	12.0	4.0	<0.001 ^a
Breast	2.4	1.2	<0.001 ^a
Colorectal	7.6	3.6	0.002 ^a
Prostate	4.4	1.4	<0.001 ^a
Cervix/uterus	9.6	-	-

^a: One-sample proportion test

Table 5. SUV_{max} values in malignant tumors confirmed by biopsy across incidentaloma localizations

Incidentaloma localization	SUV _{max}		p value
	Mean ± SD	Median (min-max)	
Thyroid	5.66±3.36	4.96 (1.95-10.78)	0.857 ^a
Colon	10.91±6.46	8.57 (4.87-20.24)	0.381 ^a
Rectum	5.09± -	5.09 (5.09-5.09)	1.000 ^a
Prostate	17.49± -	17.49 (17.49-17.49)	1.000 ^a
Cervix/uterus	7.28±3.14	7.00 (3.63-10.80)	0.333 ^a
Breast	3.02± -	3.02 (3.02-3.02)	1.000 ^a

SD: Standard deviation, Min: Minimum, Max: Maximum, ^a: Mann-Whitney U test, SUV_{max}: Maximum standardized uptake value

Table 6. Univariate and multivariate logistic regression analysis results for risk factors affecting malignancy

Variables	Univariate			Multivariate		
	OR	95% CI (min-max)	p value	OR	95% CI (min-max)	p value
Age	0.971	0.913-1.033	0.350	0.964	0.897-1.037	0.322
Gender (Female)	1.385	0.213-8.983	0.733	2.132	0.283-16.019	0.462
SUV _{max}	0.957	0.822-1.113	0.566	0.990	0.831-1.180	0.915

OR: Odds ratio, CI: Confidence interval, Min: Minimum, Max: Maximum, SUV_{max}: Maximum standardized uptake value

Discussion

Incidentalomas are lesions detected incidentally on imaging performed for unrelated clinical indications. With increasing use of ¹⁸F-FDG PET/CT, detection of PAIN (PET-PAIN) has become more frequent. PAIN is most commonly observed in the thyroid, gastrointestinal tract, and lungs, with a reported cumulative incidence of 1-3% (2).

In our study, the overall rate of incidentalomas was slightly below the lower limit reported in the literature, with the thyroid being the most common site (11.6%). Previous reports suggest that 27-44% of all malignancies diagnosed incidentally on PET/CT originate from the thyroid gland (1). Thyroid uptake can appear as either diffuse or focal activity; diffuse uptake is associated with inflammatory conditions, whereas focal uptake is more frequently linked to nodular pathology. The reported incidence of focal thyroid uptake on ¹⁸F-FDG PET/CT ranges from 2-4%, with an associated

risk of malignancy of 20-30% (3). Larger cohort studies report variability in malignancy rates, ranging from 9.8% to 28% (6,7), which likely reflects differences in the patient populations selected for further evaluation. For example, while Chen et al. (8) reported a 14% malignancy rate with 83% of patients undergoing biopsy, another study found a 42% malignancy rate in a cohort where only 11% underwent biopsy (9). A review of more recent data reveals that Lee et al. (10) identified thyroid incidentalomas in 2.7% of patients, with a malignancy rate of 56.5% among these lesions.

In our study, 37.6% of patients underwent further imaging, and 24.1% underwent biopsy; malignancy was found in 85.7% of those biopsied. This high rate likely reflects a preselection bias favoring patients with higher clinical suspicion. Nonetheless, such a high malignancy rate may contribute to clinical uncertainty regarding which patients

warrant further investigation or biopsy. This ambiguity can result in either unnecessary procedures or missed malignancy diagnoses. Therefore, patients with focal or unilateral thyroid uptake should be prioritized for further evaluation (1). Physical examination remains essential; malignancy rates were 24% in patients with thyroid-related findings on examination versus only 6% in those without. This underscores the importance of thorough physical assessment when thyroid incidentalomas are detected. While data on diffuse uptake are limited because biopsy is rarely performed in such cases, at a minimum, an ultrasonographic evaluation is advisable.

Breast incidentalomas are rare findings on PET/CT (2). In our cohort, they accounted for 2.4% of incidentalomas, the lowest rate observed. Notably, 62.5% of these cases represented primary breast malignancies. Panareo et al. (2) reported a 1.17% prevalence of breast incidentalomas among 3,675 patients undergoing PET/CT for non-breast malignancies; 15 of the 22 biopsied cases were malignant. Menon and Bourke (11) reported a malignancy risk of 56.2% for breast incidentalomas. In contrast, we observed a lower rate (33.3%), which may be attributable to the effectiveness of national breast cancer screening programs in Türkiye. In patients undergoing regular screenings with no significant risk factors, a more conservative approach may be appropriate.

The incidence of prostate incidentalomas has been reported as 0.086-1.4% (5). These lesions may represent prostate cancer, benign prostatic hyperplasia, or prostatitis. In our study, 63.6% of patients with prostate incidentalomas underwent further investigation, and 83.3% of these were found to have malignancy—a rate significantly higher than previously reported [5.4% by Han et al. (12) and 12.5% by Bertagna et al. (13)]. Bertagna et al. (13)]. These findings raise concerns about the 36.3% of patients who were not investigated further and highlight the need for heightened clinical vigilance and multidisciplinary collaboration in managing such cases.

Colon and rectal incidentalomas were observed in 7.6% and 2.0% of patients, respectively. Further investigations were conducted in 78.9% of colonic cases and in all rectal cases. A meta-analysis by Treglia et al. (4) reported a combined prevalence of 3.6% for focal colorectal incidentalomas, suggesting that our findings are higher. In our study, colonoscopic evaluation revealed malignant or premalignant lesions in 71.4% of colonic and 50.0% of rectal incidentalomas—the former slightly exceeding rates reported in the literature (68-69.5%) (4,14). This underscores the importance of a cautious approach to

incidental colorectal uptake. Clinicians should also be mindful of physiological uptake patterns in the colon that could obscure malignant lesions. Endoscopic evaluation is warranted for all focal uptakes, even in the absence of morphological abnormalities.

Incidental uterine or cervical uptake was observed in 9.6% of patients—higher than that observed in the breast, prostate, colon, or rectum. However, existing literature offers limited data on these localizations. In our study, 70.8% of such cases underwent further assessment, and malignancy was confirmed in 83.3% of those assessed. These findings highlight the importance of increased awareness and more structured evaluation protocols for uterine/cervical incidentalomas.

SUV_{max} is often considered in clinical decision-making. However, it is influenced by tumor biology and various technical factors. Although multiple studies have attempted to establish SUV_{max} thresholds, results remain inconsistent in distinguishing between benign and malignant lesions (15-17). Consequently, SUV_{max} should not be used as a standalone predictor of malignancy. In recent years, studies have indicated that SUV_{max} serves as a valuable prognostic marker in patients with a confirmed diagnosis of malignancy (18-20). However, based on the findings of this study, SUV_{max} does not reliably distinguish benign from malignant lesions when histopathological confirmation is lacking.

Study Limitations

This study has several limitations. Patients with incidental uptake who were not evaluated further may have been inadvertently excluded. Additionally, not all patients underwent biopsy, potentially introducing selection bias in malignancy rate estimates.

Conclusion

This study highlights the importance of further evaluation of incidental uptakes detected by ^{18}F -FDG PET/CT and the need for tissue diagnosis based on the characteristics of the lesions. Unlike other imaging modalities, PET/CT provides comprehensive information by evaluating the entire body rather than focusing on a specific region. Incidental findings outside the primary malignancy site occur with a notable frequency and should not be underestimated. For clinicians, awareness of such findings is crucial in identifying patient groups who may require further diagnostic work-up and treatment.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of University of Health Sciences Türkiye, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital under the (number: 2024-10/148, date: 31.10.2024).

Informed Consent: This study has been reviewed retrospectively.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.K., D.B., A.H.U., Concept: Y.K., D.B., A.H.U., G.U., Design: Y.K., D.B., Data Collection or Processing: Y.K., D.B., Analysis or Interpretation: Y.K., A.H.U., Literature Search: Y.K., G.U., Writing: Y.K., D.B., A.H.U., G.U.

Conflict of Interest: No conflict of interest was declared by the authors.

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